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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/672,335	09/28/2000	Joseph M. Cummins	5523-67250	7680

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	6

DATE MAILED: 10/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/672,335	CUMMINS ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *1-23 and 29-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600

Claims 1-33 are pending.

Applicant's election without traverse of Group IV, Claims 24- 28 in Paper No. 5 is acknowledged.

Claims 1-23 and 29-39 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 24-28 are under consideration in the instant application.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical formulation, comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma for treatment acute inflammation and acute and quiescent phase of murine *Mycobacterium tuberculosis* infection, does not reasonably provide **enablement** for a pharmaceutical formulation comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma for treatment any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses that orally administered low-dose INF-gamma in mice model decrease the severity of acute inflammation (Example 4 of the specification as filed) and acute and quiescent phase of murine *Mycobacterium tuberculosis* infection (Example 5 of the specification as filed).

The specification does not adequately teach how to effectively treat any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis or reach any therapeutic endpoint in mammals by administrating a pharmaceutical formulation, comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma. Moreover, no animals were used as model system to treat any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis. It is not clear that reliance on the *in vivo* data of reduction in neutrophil migration after administrating a pharmaceutical formulation, comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma accurately reflects the relative mammal efficacy of the claimed therapeutic strategy. The specification does not teach how to extrapolate data obtained from limited *in vivo* assay studies to the development of effective *in vivo* mammalian therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the pharmaceutical formulation comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma exemplified in the specification.

However, an effective protocol for the treatment for a bacterial, fungal diseases, monocytes, neutrophil or B cell dysfunction, cancer and fibrosis in mammalian is subject to a number of factors which enter the picture beyond simply the administration of the therapeutic composition in an acceptable formulation. Demonstrating that orally administered low-dose INF-gamma in mice model decrease the severity of acute inflammation (Example 4 of the specification as filed) and acute and quiescent phase of murine *Mycobacterium tuberculosis* infection (Example 5 of the specification as filed) cannot alone support the predictability of a pharmaceutical formulation comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma for treatment any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis through administration of the appropriate formulation. Van Noort et al. (International Review of Cytology, 1998) indicate factors that effect autoimmune disease such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to suppress and thereby treat bacterial, fungal diseases, monocytes, neutrophil or B cell dysfunction, cancer and fibrosis will vary depending upon factors such as the condition of the host and burden of disease.

The specification does not provide sufficient teaching as to how it can be assessed that treatment of any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis was achieved after the administration of a pharmaceutical formulation, comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed pharmaceutical formulation comprising in unit dosage form about 10 to about 50,000 IU of human INF-gamma for treatment any bacterial, any fungal diseases, any monocytes, neutrophil or B cell dysfunction, any cancer and any fibrosis in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cummins (US Patent NO: 5,019,382)

Cummins teaches a pharmaceutical formulation, comprising a low dosage from about 1 to about 15,000 IU of human IFN-gamma and a pharmaceutically acceptable carrier. (see entire document, Abstract , column 2, line 65 and column 13, line 46 in particular). Cummins also teach that said pharmaceutical formulation can be in liquid or solid form (column 13, lines 40-65) , or saliva-soluble form (see Abstract in particular) or formulation in lozenge dosage form (column 13, lines 20-40). Cummins teaches that said pharmaceutical formulation can be useful

for treatment of neoplastic disease, hyperallergenicity, autoimmune disorders characterized by chronic tissue degenerative inflammation and immuno-resistant viral infections , infectious disease of viral origin in human, canine and feline species (see Abstract and Claim 1 in particular).

Cummins does not explicitly teaches that a pharmaceutical formulation, comprising a low dosage from about 10 to about 50,000 IU of human IFN-gamma.

The claimed dosage from about 10 to about 50,000 IU of human IFN-gamma overlaps the referenced low dosage from about 1 to about 15,000 IU of human IFN-gamma and is therefore an obvious variation of the reference teaching absent a showing of unobvious property. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

5. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cummins (US Patent NO: 5,019,382)as applied to claims 24-27 above, and further in view of Schlom et al., (US Patent NO; 6,045,802) or Goeth et al., (US Patent NO: 5,178,857).

The teaching of Cummins has been discussed, supra.

Cummins does not teach a pharmaceutical formulation comprising of human IFN-gamma and a therapeutic agent selected from a group consisting of an antibiotic, an antifungal, an antifibrotic and a chemotherapeutic agent known for use in cancer therapy or for treatment of immune diseases characterized by hypoactive or hyperactive immune system dysfunction.

Schlom et al., teach a combination therapy, wherein a pharmaceutical composition comprises combination of INF-gamma and immunomodulators or immunostimulators, chemotherapeutic drugs, antibiotics, antifungal drugs and antiviral drugs (see entire document, column 13, line 9-25 in particular) and pharmaceutically acceptable carrier.

Similarly, Goeth et al., teach combine therapy, wherein a pharmaceutical composition comprises combination of INF-gamma and antibiotics (see entire document, Abstract in particular). Goeth et al., also teach that combine therapy is more efficient than monotherapy using INF gamma alone (column 4, line 45-50 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Schlom et al., or Goeth et al., to those of Cummins to obtain a

claimed a pharmaceutical formulation comprising of human IFN-gamma and a therapeutic agent selected from a group consisting of an antibiotic, an antifungal, and a chemotherapeutic agent known for use in cancer therapy or for treatment of immune diseases characterized by hypoactive or hyperactive immune system dysfunction.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because combination therapy, wherein a pharmaceutical composition comprises combination of INF-gamma and immunomodulators or immunostimulators, chemotherapeutic drugs, antibiotics, antifungal drugs and antiviral drugs and pharmaceutically acceptable carrier is more efficient than monotherapy using INF gamma alone as taught by Schlom et al., or Goeth et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. No claim is allowed.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
October 21, 2002

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